

021588-5002

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER(S)**

**21-588/S-002**

**Trade Name:** Gleevec

**Generic Name(s):** (imatinib mesylate)

**Sponsor:** Novartis Pharmaceuticals, Corp.

**Agent:**

**Approval Date:** December 8, 2003

**Indication:** Provides for revised package insert to fulfill post-marketing commitment #2

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APPLICATION NUMBER:

21-588/s-002

## CONTENTS

### Reviews / Information Included in this NDA Review.

Approval Letter	X
Approvable Letter	
Final Printed Labeling	X
Medical Review(s)	X
Chemistry Review(s)	
EA/FONSI	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/ Biopharmaceutics Review(s)	
Administrative Document(s)	X
Correspondence	X

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**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**21-588/S-002**

**Approval Letter(s)**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-588/S-002

Novartis Pharmaceuticals Corporation  
One Health Plaza, Building 105/2W200  
Hanover, New Jersey 07936-1080

Attention: Robert A. Miranda, Director  
Drug Regulatory Affairs

Dear Mr. Miranda:

Please refer to your supplemental new drug application dated August 26, 2003, received August 28, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Gleevec® (imatinib mesylate) Tablets, 100 mg and 400 mg.

We acknowledge receipt of your submissions dated December 20, 2002 (to NDA 21-335), October 7, 2003 and your correspondence dated November 24, 2003.

This supplemental new drug application provides for a revised package insert with updated data and fulfills the prior accelerated postmarketing commitment #2 under NDA 21-588/N-000 "To provide interval follow-up information on studies 102, 109 and 110" for the use of Gleevec (imatinib mesylate) Tablets for the treatment of patients with Philadelphia chromosome positive chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-588/S-002." Approval of this submission by FDA is not required before the labeling is used.

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills your accelerated approval commitments made under 21 CFR 314.510 for the treatment of patients with Philadelphia chromosome positive chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

We note that we are releasing you from the following accelerated approval postmarketing commitment under NDA 21-588/N-000 for the treatment of patients with Philadelphia chromosome positive chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

Commitment #1: To conduct and submit the final study report for Protocol 106 entitled "A phase III study of STI571 versus Interferon- $\alpha$  (IFN- $\alpha$ ) combined with Cytarabine (Ara-C) in patients with newly diagnosed previously untreated Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia in chronic phase (CML-CP)" with Time to Progression (TTP) as the primary surrogate endpoint. TTP is defined as any of the following: loss of complete hematologic response (CHR), loss of cytogenetic response, inability to maintain peripheral blood counts, increasing organomegaly, accelerated phase CML, blast crisis, or death from CML.

We remind you of your open postmarketing study commitments. These commitments are listed in the November 6, 2003 postmarketing commitment letter. We note that the open accelerated approval commitment #7 under NDA 21-588/N-000 for newly diagnosed adult patients with Philadelphia chromosome positive chronic myeloid leukemia (CML) in chronic phase is the subject of Protocol 106.

Commitment #7: To provide interval follow-up safety and efficacy information on study 106 annually, for three additional years, and survival data and serious adverse event data thereafter for another three years. Timeline: First interval report expected January 2004 and annually thereafter until January 2009.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Ann Staten, Regulatory Project Manager, at (301) 594-0490.

Sincerely,

 *(See appended electronic signature page)*

Richard Pazdur, M.D.

Director

Division of Oncology Drug Products

Office of Drug Evaluation I

Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Richard Pazdur :  
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